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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,918	05/10/2001	Stanley R. Krystek	DB24NP/30436.46USU1	7606

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EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 11/05/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/853,918	Applicant(s) KRYSTEK ET AL.	
	Examiner Yong Pak	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *7,10,14-31,33-52 and 54-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-9,11-13, 32 and 53* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6-8,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-56 are pending.

Election/Restrictions

Applicant's election without traverse of Group I (1-17, 32, 53 and 55-56) in Paper No. 10 is acknowledged. Mr. Lange made a further election to prosecute the mutant dehydrogenase of SEQ ID NO:30 as shown in Figure 17.

Claims 7, 10, 14-31, 33-52 and 54-56 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claim Objections

Claims 8-9, 11-13, 32 and 53 are objected for being drawn to non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-6, 9 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 are drawn to mutant IMPDH of any structure and from any source. Claims are also drawn to more than one isoform of the enzyme. Since there is no limit to structure or source of the enzyme, the claim encompasses a genus of molecules described by the function of being a IMPDH enzyme. There is also no limit to the structure of the oligopeptide and no limit to the region of the wild type IMPDH wherein the oligopeptide is substituted. The specification does not describe which amino acids of a wildtype IMPDH can be deleted, substituted, added or inserted and still impart the mutant protein with IMPDH activity. Therefore, the specification fails to describe representative species by any identifying characteristics other than the functionality of being an IMPDH.

Claims 4-5, 9 and 11-13 limit the invention to a an array of tri-peptides. However, there is no limit to the region of the wild type IMPDH wherein the oligopeptide is substituted. The specification does not describe which amino acids of a wildtype IMPDH can be deleted, substituted, added or inserted and still impart the mutant protein with IMPDH activity. Therefore, the specification fails to describe representative species by any identifying characteristics other than the functionality of being an IMPDH.

Given this lack of the description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would

recognize that applicants were in possession of the inventions of claim 48, with dependent claims Claim 1-6, 9 and 11-13.

Claims 1-6, 9 and 11-13, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the mutant IMPDH of SEQ ID NO:30, does not reasonably provide enablement for a mutant IMPDH with an unlimited structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims are drawn to mutant IMPDH having unlimited structure and derived from any source. Despite knowledge in the art for isolating polypeptides, the specification fails to provide guidance regarding which amino acids of IMPDH from any source and of any isoform are required to impart a polypeptide as an IMPDH. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The specification, as discussed above which places no limit to the source or structure of the mutant IMPDH, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting IMPDH activity; (B) the general tolerance to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for substitutions, deletions, insertions/additions or multiple modifications, as encompassed by the instant claims. Also, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Therefore, one of ordinary skill would require guidance in order to make mutant IMPDH with structures different from SEQ ID NO:30 in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-7 and 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-6, 8-9, 11, 32 and 53, the mere recitation of the name "IMPDH" is insufficient to convey with clarity that which applicant sees as the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 11-13 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. in view of Gibco BRL Products Catalog.

Zhang et al. teach several bacterial/mammalian sequence signatures involved in subunit interactions, the active site flap and the NAD binding region (abstract, page 537). Because bacterial IMPDH enzymes are different from mammalian IMPDH in biochemical and kinetic characteristics, IMPDH is an attractive target for developing highly specific inhibitors (abstract page 537). Zhang et al. teach that the identification of catalytic regions refines the selection process and increases the probability that a signature sequence will be useful for the development of specific bacterial or mammalian IMPDH inhibitors (page 538). Zhang et al. teach that mutations of specific amino acids residues in the signature region and correlation of altered biochemical and kinetic characteristics can be used to elucidate the role of these amino acids in the catalytic mechanism (page 538-539).

The difference between the reference of Zhang et al. and the instant invention is that the reference of Zhang et al. does not teach how to mutagenize IMPDH to arrive at a more refined signature region.

Methods of mutagenesis are well known and practiced in the art. Gibco BRL Products Catalog (95-96) teaches how to perform site-specific mutagenesis (page 18-33)

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to mutagenize wildtype IMPDH involving substitutions or deletions of amino acids to arrive at a more refined bacterial or mammalian signature motif. The motivation of making such mutants is to increase the probability that a signature sequence will be useful for the development of specific bacterial/mammalian IMPDH inhibitors. One of ordinary skill in the art would have had a reasonable expectation of success since site-specific mutagenesis is performed routinely in the art.

No claims are all owed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 8:00 A.M. to 4:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

October 24, 2002

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